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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/758,902	01/16/2004	Fiorenzo Stirpe	PNJ-005CNRCE	7360

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EXAMINER	
SWOPE, SHERIDAN	
ART UNIT	**PAPER NUMBER**
1652	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/758,902	STIRPE ET AL.	
	Examiner	Art Unit	
	Sheridan L. Swope	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 August 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-20,27,30,33 and 36-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-20,27,30,33 and 36-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' response on August 9, 2007, to the Action on the Merits of this case mailed October 12, 2006, is acknowledged. It is acknowledged that applicants have cancelled Claims 28, 29, 31, 32, 34, and 35, amended Claims 11, 15, and 17, and added Claims 37-48. Claims 11-20, 27, 30, 32, and 36-48 are pending. New Claims 37-48 are encompassed by the elected invention. Claims 11-20, 27, 30, 33, and 36-48 are hereby considered.

Information Disclosure Statement

As stated previously, JP-1-272599 listed on the Information Disclosure Statement filed September 19, 2006 has not been considered because it is in Japanese. If Applicants wish for JP-1-272599 to be considered, a translation should be submitted.

Claim Rejections - 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Rejection of Claims 11-20 and 27 under 35 U.S.C. 112, first paragraph lack of enablement, for essentially the same reasons stated in the prior actions, is maintained. New Claims 37-42 are herein rejected under 35 U.S.C. 112, first paragraph lack of enablement. The specification is enabling for making and using an isolated *B. spectabilis* polynucleotide comprising SEQ ID NO: 8 or encoding a polypeptide comprising SEQ ID NO: 9, wherein the encoded polypeptide has RIP activity. However, the specification fails to enable the skilled artisan to make and use any polynucleotide encoding a polypeptide comprising a sequence at

least 75% identical to SEQ ID NO: 9, wherein the polynucleotide encodes a protein with RIP activity. The specification also fails to enable the skilled artisan to make and use any polynucleotide comprising SEQ ID NO: 8 or encoding a polypeptide comprising SEQ ID NO: 9, wherein the encoded polypeptide has any or no activity. In support of their request that said rejection be withdrawn, Applicants provide the following arguments.

(A) Disclosure *a priori* of the full-length amino acid sequence and corresponding nucleic acid coding sequence of bouganin RIP is not required to meet the enablement requirement. The skilled artisan, provided with the disclosed information, would understand how to make and use the invention without undue experimentation.

(B) Hartog et al, 2002 [den Hartog] discloses the cloning of the complete nucleotide and protein sequences of bouganin using teachings of the specification.

(C) The functional and structural information disclosed in the instant application demonstrates that Applicants were in possession of a novel member of a protein family having RIP activity.

These arguments are not found to be persuasive for the following reasons.

(A) Reply: It is acknowledged that disclosure of SEQ ID NO: 8 and 9 by the specification enables the skilled artisan to make and use an isolated *B. spectabilis* polynucleotide comprising SEQ ID NO: 8, wherein the polynucleotide encodes a polypeptide comprising SEQ ID NO: 9 and having RIP activity. However, the specification fails to enable the skilled artisan to make and use any polynucleotide encoding a polypeptide comprising a sequence at least 75% identical to SEQ ID NO: 9, wherein the polynucleotide encodes a protein having RIP activity. The specification also fails to enable the skilled artisan to make and use any polynucleotide

comprising SEQ ID NO: 8 or encoding a polypeptide comprising SEQ ID NO: 9, wherein the encoded polypeptide has any or no activity. As explained in the prior actions, the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the results of such modifications are unpredictable (Galye et al, 1993; Whisstock et al, 2003). In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

Claims 11-20 and 27 are so broad as to encompass any polynucleotide encoding a polypeptide comprising a sequence at least 75% identical to SEQ ID NO: 9, wherein the polynucleotide encodes a protein with RIP activity. Claims 37-42 are so broad as to encompass any polynucleotide comprising SEQ ID NO: 8 or encoding a polypeptide comprising SEQ ID NO: 9, wherein the encoded polypeptide has any or no activity. The specification does not support the broad scope of Claims 11-20, 27, and 37-42 because the specification does not establish: (A) the function of all proteins comprising SEQ ID NO: 9 or encoded by a polynucleotide comprising SEQ ID NO: 8; (B) regions of the protein structure which may be modified without affecting the desired activity; (C) the general tolerance of the desired activity to modification and extent of such tolerance; (D) a rational and predictable scheme for modifying any residues with an expectation of obtaining the desired biological function; and (E) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of the identity of sequences having the desired biological characteristics

is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

(B) Reply: Since den Hartog et al, 2002 was published prior to publication of the instant application, December 30, 2004, den Hartog et al could not have relied on the instant disclosure for their teachings.

(C) Reply: This argument seems more appropriate for the Written Description rejection; see below. It is acknowledged that Applicants were in possession of a novel isolated protein having RIP activity. Said invention was issued as US 6,680,296. It is also acknowledged that Applicants were in possession of 50% of the polynucleotide coding sequence (SEQ ID NO: 8). However, possession of an isolated protein, or a polynucleotide fragment, is not possession of a polynucleotide encoding a full-length polypeptide having the desired activity, as recited in the instant claims. See MPEP 2163(II)(A)(3)(a) which states:

> 'A definition by function alone "does not suffice" to sufficiently describe a coding sequence "because it is only an indication of what the gene does, rather than what it is." *Eli Lilly*, 119 F.3 at 1568, 43 USPQ2d at 1406. See also *Fiers*, 984 F.2d at 1169-71, 25 USPQ2d at 1605-06.'
>
> And
>
> '...disclosure of only a method of making the invention and the function may not be sufficient to support a product claim other than a product-by-process claim. See, e.g., *Fiers v. Revel*, 984 F.2d at 1169, 25 USPQ2d at 1605'.

For these reasons and those explained in the prior actions, Claims 11-20, 27, and 37-42 are rejected under 35 U.S.C. 112, first paragraph lack of enablement.

Written Description

Rejection of Claims 11-20, 27, 30, 33, and 36 under 35 U.S.C. 112, first paragraph insufficient written description, for the reasons stated in the prior action, is maintained. Claims

43-48 are rejected under 35 U.S.C. 112, first paragraph insufficient written description, for the reasons. Claims 43-48 recite a genus of polynucleotides encoding a polypeptide comprising SEQ ID NO: 9, wherein the polypeptide has RIP activity. The specification discloses not species of said genus. Therefore, the subject matter was not described in such a way as to reasonably convey to one skilled in the relevant art that the Inventors, at the time the application was filed, had possession of the claimed invention.

In support of their request that said rejection be withdrawn, Applicants provide the following arguments. Also see (C), above.

(D) The written description requirement does not require the specification to disclose each and every embodiment encompassed by a claim, but that the skilled artisan be enabled to make and use the encompassed embodiments without undue experimentation.

(E) The amended claims recite polynucleotide encoding proteins comprising a sequence having at least 75% homology to SEQ ID NO: 9.

These arguments are not found to be persuasive for the following reasons.

(D) Reply: This argument, which is relevant to the enablement rejection not written description, is the same argument Applicants provided in their response of July 18, 2006. Applicants are referred to the Office's reply of October 12, 2006.

(E) Reply: As explained in the prior rejection of October 12, 2006, recitation of the limitation of a polynucleotide encoding a protein comprising a polypeptide having at least 75% homology to SEQ ID NO: 9 is introduction of New Matter. Applicants have failed to provide evidence that said limitation is disclosed in the Application.

For these reasons and those explained in the prior actions, rejection of Claims 11-20, 27, 30, 33, and 36 under 35 U.S.C. 112, first paragraph insufficient written description, is maintained.

Claims 37-42 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the Inventors, at the time the application was filed, had possession of the claimed invention. These claims are directed to a genus of polynucleotides either comprising SEQ ID NO: 8 or encoding a polypeptide comprising SEQ ID NO: 9, wherein the encoded polypeptide has any or no activity. The specification does not contain any disclosure of the function of all said polynucleotides. The genus of nucleic acid molecules that comprise these above polynucleotides is a large variable genus with the potentiality of encoding many different proteins. Therefore, many functionally unrelated polynucleotides are encompassed within the scope of these claims, including partial nucleic acid sequences. The specification discloses the function of no species of the claimed genus, which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Allowable Subject Matter

No claims are allowable.

Applicant's amendment necessitated any new grounds of rejection presented in this Office action. Any new references were cited solely to rebut Applicants' arguments. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Regarding filing an Appeal, Applicants are referred to the Official Gazette Notice published July 12, 2005 describing the Pre-Appeal Brief Review Program.

Final Comments

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants' remarks, requests for extension of time, and any other distinct papers be submitted on separate pages.

It is also requested that Applicants identify support, within the original application, for any amendments to the claims and specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published application may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on the access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sheridan Lee Swope, Ph.D.
Art Unit 1652

SHERIDAN SWOPE, PH.D.
PRIMARY EXAMINER